Medicine and Books

Disordered immunity in the nervous system

Current Topics in Immunology. No 17. "Immunology of the Nervous System." S Leibowitz and R A C Hughes. (Pp 304; £22·50.) Edward Arnold. 1983.

The rate at which data are accumulating about disordered immunity in the nervous system and its appendages is reflected in the rapidly expanding number of publications on the subject. Thus, not surprisingly, we have been provided with yet another update, on this occasion in the "Current Topics in Immunology" series edited by Professor J L Turk from the Royal College of Surgeons. In this compact and well organised volume Dr Sidney Leibowitz and Dr R A C Hughes have produced a comprehensive and profusely illustrated account of the particular features of immune responses in the central nervous system, conditioned as they are by the blood-brain barrier and immunological aspects of the more commonly encountered disorders such as multiple sclerosis, the Guillain-Barré syndrome, and myasthenia gravis. In addition, they review the neurological and neuromuscular manifestations of systemic disorders such as rheumatoid arthritis and lupus erythematosus and conclude with a succinct discussion of tumour immunity in the context of the central nervous system and the application of modern immunological techniques, particularly immunocytochemistry, to the study of neurobiology.

I found the sections devoted to the experimental allergic inflammatory disorders of the central and peripheral nervous systems and their possible relationship to human disease particularly illuminating and indicative of the authors' considerable experience. Discussing experimental allergic encephalomyelitis they recall the historical basis for this model in the series of so called "neuroparalytic accidents" consequent upon vaccination against rabies with Pasteur's vaccine. Noting the close analogy between the human and experimental disorders in this context, they go on to emphasise the central role of myelin basic protein as the encephalitogenic antigen in allergic encephalomyelitis and how its development can be prevented or suppressed by immunising the animals with synthetic copolymer with a composition resembling myelin basic protein itself. Leibowitz and Hughes also note the close resemblance between the histological lesions in the chronic relapsing model of allergic encephalomyelitis and human demyelinating disease. Quite properly, however, they warn against "going over the top" in extending this analogy. In the chapter devoted to the allergic neuritides, they show some morphological similarities between experimental allergic neuritis and the Guillain-Barré group of neuropathies in man. Nevertheless, the two conditions behave in different ways and the analogy between allergic neuritis and the chronic relapsing polyneuritis in man is likely to be closer, a point underlined by the steroid responsiveness of the latter (Guillain-Barré syndrome is not helped and may be made worse by corticosteroid steroids as evidenced by the only controlled studies published thus far—the results of the multicentre trials of plasmapharesis are awaited with interest). This section includes a useful review of the clinical as well as the immunological features of the Guillain-Barré syndrome.

From the clinical neurologist's standpoint the two most important contributions are those dealing with multiple sclerosis and myasthenia gravis. In the former the authors stand history on its head by referring to "plaque en sclerose" (Charcot's essay was entitled "Sclerose en plaques disseminées") but otherwise give an excellent account of the aetiology and pathogenesis of this condition, including the possible role of slow viral infection in childhood and early adolescence and autoimmunity mediated by immunocomponent cells crossing the blood-brain barrier from the circulation. Cogently they argue against uncritical acceptance of the autoimmune hypothesis and allergic encephalomyelitis in either its acute or chronic forms as a model of the human disease in the absence of unequivocal evidence of an immune response to myelin antigens in cerebrospinal fluid or blood.

In contrast to multiple sclerosis, myasthenia gravis stands out as a paradigm of organ specific autoimmune disease and the authors recount the dramatic developments in understanding its pathogenesis during the past decade. The following points may be regarded as quibbling but an earlier mention of Iain Simpson's pioneering contribution might have been appropriate in this section and presumably the authors mean "thymic hyperplasia" when discussing the operative findings in myasthenia gravis (p 148). In addition, personal prejudice dictates a preference for the primacy of complement mediated lysis in the pathogenesis of the endplate lesions in myasthenia gravis and less ambivalence about thymectomy, particularly at an early stage in its clinical course. Discussing the experimental model, it is perhaps surprising that they did not comment further on "the most striking feature" of this condition, which is "cellular infiltration . . ." of the endplate region. This feature is conspicuous by its absence in the human disease and inevitably raises doubts about the comparability of the two processes.

The remaining chapters consider the role of immunological dysfunction in a variety of disorders of the central nervous system, and the neuromuscular apparatus, including conditions which are not regarded as primarily "immunological." For example, they discuss putative infections such as Creutzfeldt-Jakob disease (not invariably accompanied by myoclonus, it should be noted) and non-infective processes such as Alzheimer's disease (characterised by granulovacuolar, not granulovascular degeneration of neurones—see their figure 10.2). In addition they furnish comprehensive reviews of the immunological aspects of the commoner infections of the central nervous system and inflammatory myopathies with or without evidence of a systemic collagen vascular disease.

This well rounded volume is likely to become a bench book for neurologists, neuropathologists, and clinical immunologists alike. Accordingly, it is disappointing that the photomicrographs have a "flat" appearance, which morphological purists are likely to find unpleasing (the line diagrams are excellent). Further, the text contains a plethora of typographical errors which would rival the *Grauniad* at its malapropian worst. None the less it remains a veritable "snip" at £22·50.

PETER HUDGSON

Do animals think?

International Library of Psychology. "Animal Thought." Stephen Walker. (Pp 437; £17·50.) Routledge and Kegan Paul. 1983.

A cat with a lesion in the locus ceruleus exhibits an extraordinary type of sleepwalking in which it "acts out" its dreams—stalking mice, preening itself, and searching for food, even while soundly asleep. Some years ago, after writing about this intriguing discovery by Michel Jouvet, I was surprised to learn that many intelligent people consider the existence of dreaming in animals to be worth neither intellectual speculation nor scientific investigation. They see it as perfectly obvious—from the twitching paws of a slumbering dog, for example—that our pets do indeed dream. Nothing more need be said; Jouvet's work merely confirms what has been known for centuries.

The opposite applies to the process of thinking, though once again we are told that there is no point in discussing the matter. As Stephen Walker observes at the beginning of his fine book, if thought is defined as something exclusively human, then that is the end of any argument. Animals do not qualify. Similarly, if thinking is necessarily linked to language, then that too puts paid to any further consideration. And if consciousness is given a Marxist definition, in terms of interaction between an individual and his/her/its social environment, then again there is little sense in pondering what a goldfish or chimpanzee is doing when it thinks.

The great strength of Dr Walker's book, written in lucid prose that will appeal to layman and undergraduate alike, is the unusual style and clarity with which it shows that these and similar proferred discontinuities between man and "other" animals do not stand up to critical scrutiny. Neither from philosophical basics (is thinking a matter of perception, memory, feeling, reasoning, awareness, reflection, abstraction, foresight, intuition, or conceptualisation?) nor from psychology, neurophysiology, or comparative neuroanatomy can we sustain such a neatly demarcated view. The evidence from this currently lively topic of research suggests instead that the mental life of animals is much more like our own than was supposed in the past. Cartesian dualism is thoroughly dead. But so too are more advanced theories which nevertheless portray animals as little more than automata.

The question of how to define thought is, of course, a thorny one, and Walker shows rare skill (for a working scientist) in dissecting out the philosophical strands of the argument. But for me there are two key elements, neither of which we are entitled to believe are exclusively human: internal mapping and abstraction. In considering the former, Dr D S Olton's recent work is particularly challenging. He has developed some categorically new versions of rat in a maze experiments that no longer allow the former ambiguity of explanation. Animals placed in the centre of a maze with several radiating spokes and food in *every* one, for example, learn very quickly to retrieve each morsel—without retracing their steps and without visiting the arms in the same order. Odour and other possible clues have been ruled out, leaving the inescapable conclusion that rats are able to build up internal, conceptual representations of the world and reflect on them. If this is not thinking, what is?

Regarding abstraction, Stephen Walker does not require experimental evidence, just clear thinking, to demolish Locke's lingering view that the ability to have ideas evolved after or in step with language. He proposes instead that rather good abstract concepts of such things as bananas existed before the development of words. "Thus chimpanzees may have the idea of a banana (and related concepts such as 'lots of bananas'), bears may have a pretty clear idea of 'honey,' and cats of 'mouse,' even if they do not have words for them." To test the hypothesis that there is indeed such a thing as prelinguistic thought, Walker suggests an investigation into psychological processes in young children, in whom ideas might occasionally run ahead of speech, or in adults deprived of language by deafness or brain damage. But he insists that the evidence thus far is that animal perception and memory should be discussed "in the same breath" as their human equivalents, notwithstanding the distinctions brought by language.

Even the most old fashioned behaviourist would find it hard to dispute Walker's conclusion, after his masterly sifting of observation and speculation, that "the relation between animal cognitive capacities and those of man is still very much an open issue, rather than one that is permanently closed because of obvious differences." But more openminded readers will be persuaded further and will find themselves in agreement with the final sentence of this excellent book: "Our organ of thought may be superior, and we may play it better, but it is surely vain to believe that other possessors of similar instruments leave them quite untouched."

A few will find this recognition of the reality of animal thought disturbing. For, though Dr Walker quite deliberately sets aside questions concerning our responsibilities towards animals, it would be foolhardy to deny the implications of his thesis for activities such as animal experimentation and factory farming. To judge by recent *BMJ* exchanges over "vivisection," the level of this often ill tempered, ill informed debate would be raised if the proponents on both sides acquainted themselves with the issues raised in *Animal Thought.*

BERNARD DIXON

Microbiological safety

Laboratory-acquired Infections. C H Collins. (Pp 277; £21.) Butterworths. 1983.

Dr Collins's excellent book is packed with well referenced information and usefully detailed recommendations based on a lifetime's practical experience and concern with problems of laboratory acquired infections and safety arrangements. All this is spiced with wry humour and commonsense comments. Although priced beyond the pocket of many of those workers who would benefit from studying it, this book should certainly be available in all laboratories dealing with infectious agents. It discusses the details and reasons behind the Howie code and other official booklets, mentioning the alternatives with their relative merits and demerits.

The first four chapters define the problem, how it is assessed, and official and unofficial reactions leading to the current classifications of pathogens and of appropriate laboratories, which are summarised. All this is well referenced up to 1981 with a few 1982 entries, though just missing the 1983 publication of the latest instalment of my own survey of clinical laboratories in Britain, which recorded eight shigella infections in 1980-1 compared with the single one in 1979 quoted in the book. There is certainly scope for improvement in some of our routine bacteriology laboratories, although typhoid has not caused trouble here on the same scale as in the USA. Chapter 5 deals in practical detail with the hazards arising from equipment and techniques, incorporating concise summaries of the precautions appropriate to each problem (such as loops, pipettes, centrifuges, and so on). There is sensible emphasis on the vital importance of basic good housekeeping (without which gadgetry alone will not provide safety). Chapter 6 gives invaluably critical discussions of "safety cabinets," their design, installation, testing, maintenance, and use—a potentially indigestible chapter relieved by touches of humour and illustrative anecdotes. Its final section mentions briefly the newer, flexible plastic isolator techniques, which are worth considering for some applications. The next two chapters provide much detailed information and useful advice on the collection, transport, and reception of infectious materials and on decontamination, including the complexities and practicalities of autoclaves and

other disposal systems, which are not to be treated lightly or taken for granted.

Chapter 9 discusses the laboratory workers themselves, their protective clothing, medical supervision, and vaccinations. It is followed by a chapter on instruction in microbiological safety which will be particularly useful to safety officers and others responsible for organising training in this branch of preventive medicine. Chapter 11 deals with the design and planning of laboratories, commenting sensibly on many points of practical importance even beyond the subject of safety itself. Here again the author's extensive working experience provides the basis for stimulating challenges to some design concepts, giving a useful set of counterarguments to help senior laboratory workers negotiating with design teams. The last chapter concisely deals with the important problems of hepatitis, typhoid, and tuberculosis. It is followed by appendices on hazard warning notices and on sources of items mentioned in the text and by a list of over 700 references.

For the beginner and the half trained this book provides answers to many questions and much wise, detailed, and practical advice. For the laboratory head and for experienced and senior staff it provides a most useful summary of information and an aide memoire of useful points to help in dealing with the misconceptions of administrators and planners. It may also be commended for attention by persons in these last categories, on whom so often depend the provision of the physical requirements for good laboratory practice, which, I agree with the author, is the key to laboratory safety.

NORMAN R GRIST

Pocket book on renal disease

Pocket Consultant. "Nephrology." P E Gower. (Pp 261; £6·95.) Grant McIntyre. 1983.

In writing a pocket book for junior doctors, students, and nurses the author must choose whether to include a wide range of information or give his readers a fuller account of a few common conditions. Dr Gower has chosen the former course, so that the book is surprisingly comprehensive for its size. On the other hand, it does not give the reader a clear understanding of the many conditions and tests that are described.

For example, take urinary infection, the commonest condition seen in nephrology and one on which Dr Gower is an authority. The section on this, strangely headed "Urinary infection and x-ray abnormalities," does not explain the rationale of bacterial counting, the significance of pure and mixed growths, or the routes of infection in catheterised patients. These omissions are particularly important, as no instructions are given for obtaining uncontaminated urine specimens or for inserting catheters. This section will do little to reduce the many misleading cultures that are still obtained or the many unnecessary courses of antibiotic treatment that are prescribed.

The commonest errors in dealing with oliguria are failure to recognise that the patient needs fluid replacement, choosing the wrong fluid for replacement, and attempting to force a diuresis in established acute renal failure. Only the first of these is adequately dealt with. Upper tract obstruction is rightly emphasised in the differential diagnosis, but it is not made clear that bladder outflow obstruction, which is much more common, usually has to be ruled out first. Catheterisation is not mentioned in this context, nor is the danger of leaving the catheter in the bladder—yet this is very often done even in patients with established oliguric renal failure.

Dr Gower mentions only at the very end of the section on acute renal failure that the "renal team" must be called early, but early referral is rightly emphasised in the section on dialysis for end stage renal failure. This is the most useful section of the book, though it is astonishing that the table of relative contraindications to haemodialysis (as opposed to continuous ambulatory peritoneal dialysis and transplantation) lists only scleroderma. Social factors, arteriosclerosis, and diabetes are not mentioned here; indeed, diabetes gets little mention elsewhere, and insulin treatment is omitted from a list of causes of hypokalaemia that includes familial periodic paralysis and Barrter's syndrome (sic).

Among the merits of the book is a liberal use of flow diagrams and tables on important topics such as the choice of drugs in renal failure and of antibiotics for various infecting organisms. There are also lists of telephone numbers for poisons information and criteria for brain death and a nomogram for calculating body surface area from height and weight. The black and white illustrations of biopsy appearances are good, although the captions of two are reversed. This is one of many examples of careless proof reading, along with numerous spelling mistakes and erroneous cross references. It was alarming to read that "the donor may be anastomosed to the bladder or the ureter of the recipient."

The book is not expensive at £6·95.

A POLAK

In brief

One of the side effects of the thalidomide controversy was the increased use of experimental animals. Considerable efforts have been made since to ensure the safe evaluation of drugs, food additives, pesticides, and other chemicals. Medical research workers today, however, are becoming caught in the crossfire between consumer protection bodies wanting complete safety in therapeutics and animal welfare groups increasingly concerned about experimentation. The proceedings of a symposium in 1982, under the auspices of the Humane Research Trust and edited by Professor Paul Turner, has as its title an important question—namely, *Animals in Scientific Research: An Effective Substitute for Man?* (Macmillan Press, £35). The facts and ideas this book contains will replace some of the myths and emotions previously used to fire controversy on this topic. Although political pressure from those opposed to animal experimentation is helping to advance the science of toxicology and hastening the development of more effective culture techniques, in vitro methods are not ready to replace animal models. Considerable research effort is still required to produce adequate alternatives and this may entail killing animals to supply materials or removing some of their body fluids. Though isolated organs, tissue and cell cultures, chemical assays, mechnical models, and computer simulations can and should be used to reduce the number of animal tests carried out, the emotional reactions of the antivivisectionists should not let us forget that the proper experimental model for man is man himself.

Contributors

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